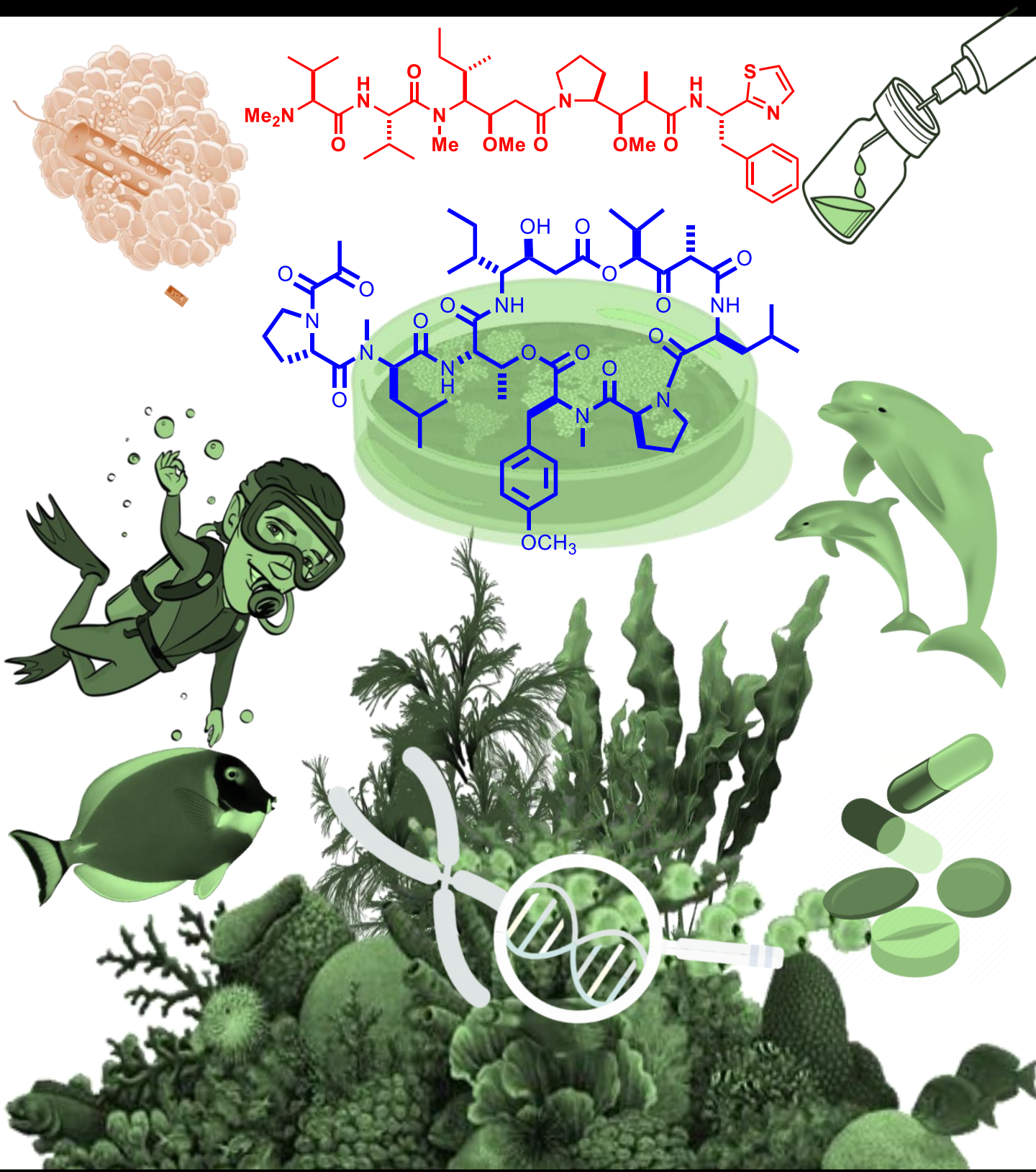
Marine Drugs

2021 – 2022 {Lecture 3}



Dr. Omar M. Sabry

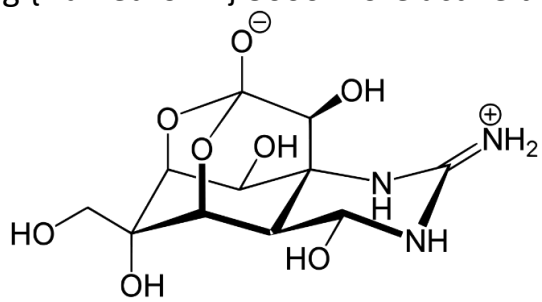
Marine Drugs

II. Marine Toxins

Toxic or poisonous substances elaborated by marine flora or fauna

❑ Tetrodotoxin (TTX)

Tetrodotoxin is a cyclic polyether nitrogenous compound {Alkaloid} isolated from puffer fish, a fish with 4 frontal teeth {Tetraodontiformes = Tetra = 4 - odonti = teeth - formes = shape}. It is also produced by other animals e.g. octopuses, salamanders and sea stars. The true producer of the compound was found to be a bacterium living in the GIT, skin, gonads and gills of the fish. Tetrodotoxin is biosynthesized from Polyketides + Guanidine group. It acts as a very strong Sodium Channel Blocker compound, leading to paralysis and respiratory collapse of the victim. Now it is approved by Health Canada as a strong analgesic drug {Halneuron™} 3000 more active than morphine.

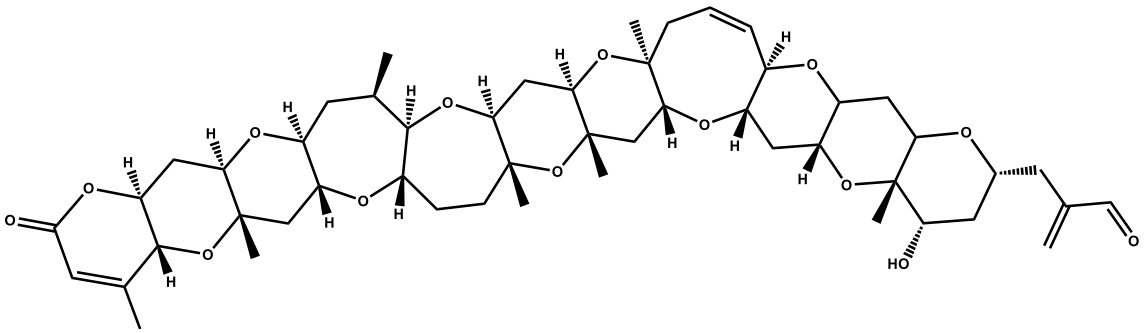


Tetrodotoxin (TTX)

❑ Brevetoxin B

Brevetoxin B is a cyclic polyether compound, biosynthesized by polyketide synthases, isolated by Japanese and American scientists at the same time in California and Japan from shellfish {Paralytic shellfish poisoning}. This compound also isolated from the true producing organism, a dinoflagellate called *Gymnodinium breve* living in symbiosis with the shellfish. It increases sodium influx {Voltage-gated sodium channel} {triggering mechanism of bronchospasm, bronchial asthma, heart problems, abdominal pain, vomiting,

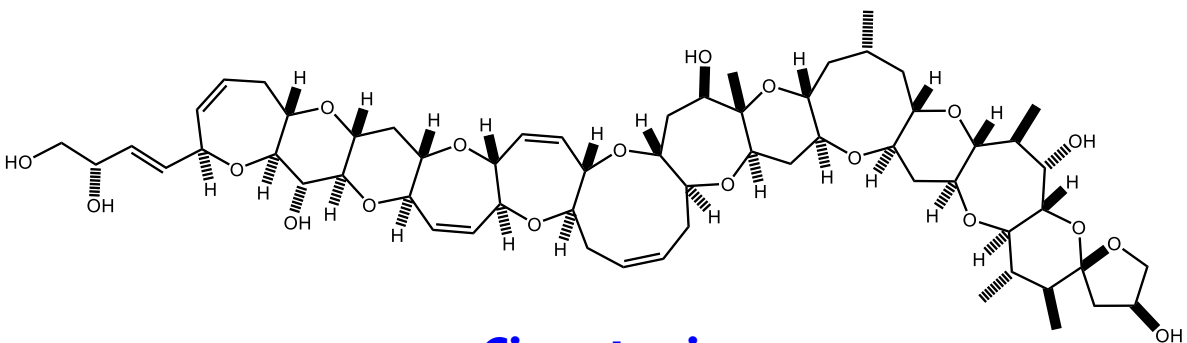
diarrhea and cardiovascular disorders}. It can be used in the syndrome of in-appropriate secretion of Anti-diuretic hormone {SIADH}



Brevetoxin B

❑ Ciguatoxin

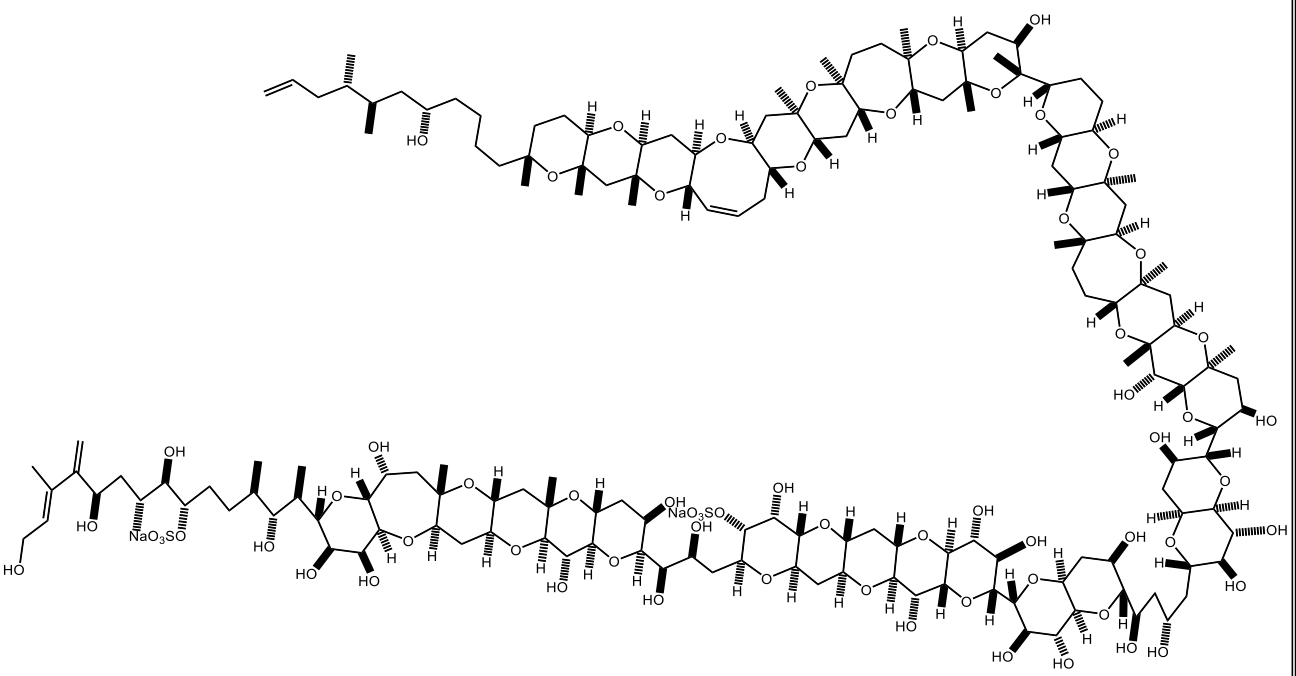
Ciguatoxin belongs to the group of marine polycyclic ether toxins implicated in Ciguatera fish poisoning. It was isolated by Japanese scientists from a Pacific moray eel then from an epiphytic dinoflagellate {*Gambierdiscus toxicus*}. It increases sodium influx {Voltage-gated sodium channel causing neurological, gastrointestinal and ionotropic cardiovascular disorders}. It can be used in syndrome of inappropriate secretion of Anti-diuretic hormone {SIADH}



Ciguatoxin

❑ Maitotoxin

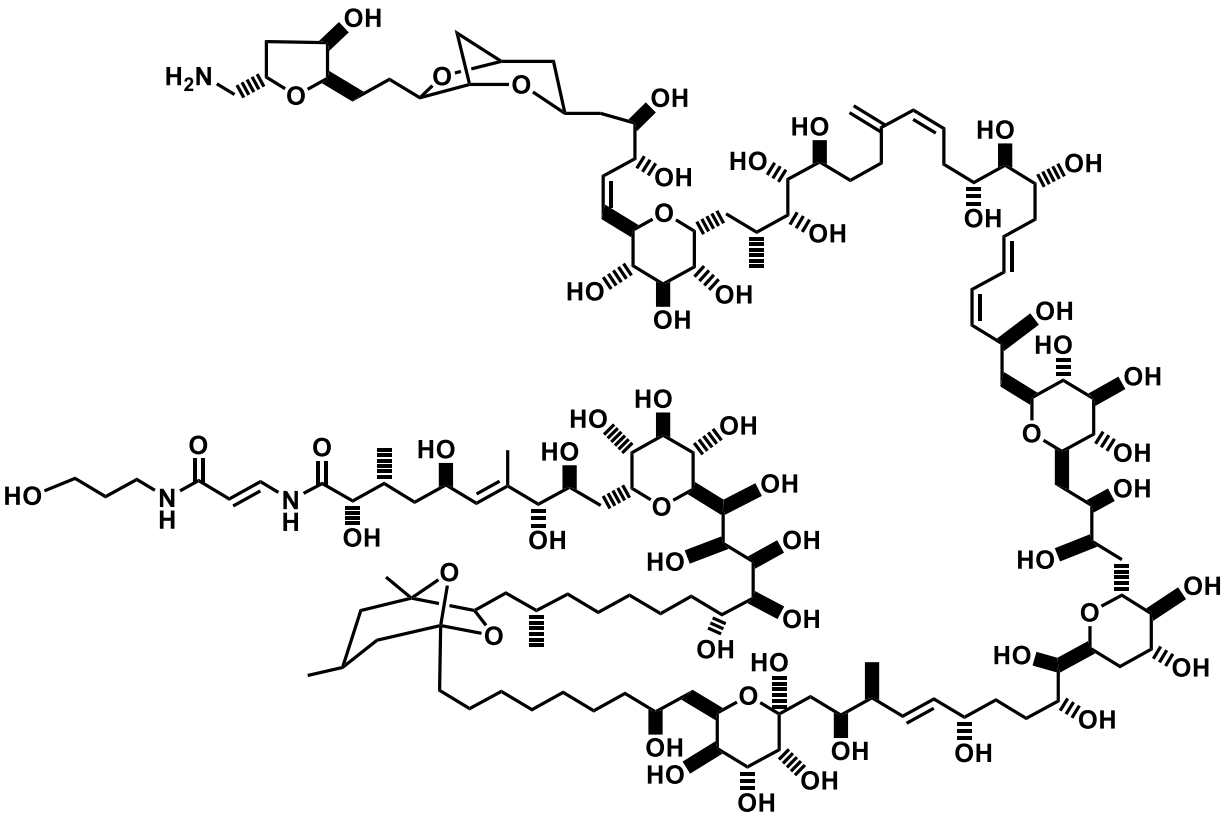
Maitotoxin (Polyether} first isolated from Maito fish. Maitotoxin exaggerates calcium influx {Voltage-gated calcium channel} causing Vasoconstriction and cardiac arrest in large dose}. In small dose it can be used as a lead drug to treatment hypotension {Cardiotonic + Vasoconstrictor}.



Maitotoxin

❑ Palytoxin

Palytoxin is the cyclic polyether {most potent toxin compound} isolated by Japanese and American scientists in the same time from a Coelenterate *Palythoa toxicus*. Palytoxin was found in a number of marine organisms. It acts by inhibition of ATPase Na^{+}/K^{+} pump also increasing Ca^{++} influx inside cells like cardiac glycosides {ionotropic and chronotropic effects - Vasoconstrictor and cardiac arrest}. Palytoxin can be used in low dose as cardiotonic {substitute of Digoxin}.



Palytoxin

❑ Jellyfish toxins

- When a jellyfish stings a person, it injects mixture of polypeptides
- These polypeptides enhance the entrance of huge amounts of potassium into neurons and normal cells {Potassium influx}
- When potassium enters the nerve cells, it affects the action potential of the cell, so the person feels as if he is burned, the desire to itch and redness of the place of the sting.

- Potassium inside the cells attracts water with it, the place of the bite is filled with water and edema appears as bruises
- **Treatment:** Zinc acetate .. Zinc closes potassium channels on the cell membrane, so potassium does not enter the cells .. acetate helps to break down polypeptides, so it does not have an effect after that.
- In low concentration Potassium is very important in regulating heart beats in arrhythmia, so Jellyfish toxins may be used in the future as lead drugs {pharmacophore} for treatment of cardiac arrhythmia by drug targeting.